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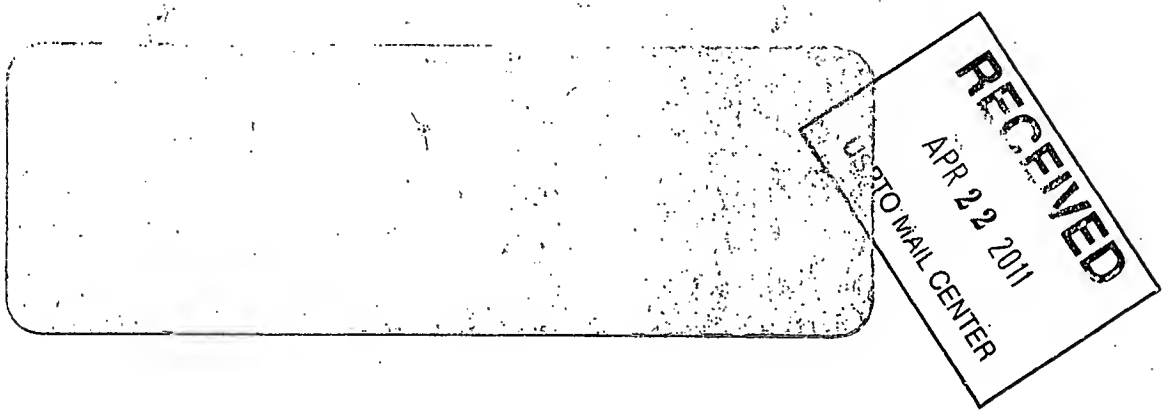

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,871	08/18/2006	Rene Roscher	27579U	3799

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NATH & ASSOCIATES PLLC
112 South West Street
Alexandria, VA 22314

EXAMINER	
CHONG, YONG SOO	
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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/589,871
Filing Date: August 18, 2006
Appellant(s): ROSCHER ET AL.

Joshua B. Goldberg
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 1/26/2011 appealing from the Office action mailed 1/5/2010.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of the claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The 103(a) obviousness rejection of claims 1, 4, 8-11, 19 as being obvious over Noe et al. (US Patent 6,613,795 B2) in view of Wurst et al. (US Patent Application 2007/0025923 A1) was made in the Final Rejection filed on 1/5/2010 as necessitated by the new claim amendments.

Appellant made new grounds of arguments in the Appeal Brief filed on 1/26/2011, which were persuasive to withdraw the 103(a) obviousness rejection

of claims 1, 4, 8-11, 19 as being obvious over Noe et al. (US Patent 6,613,795 B2) in view of Wurst et al. (US Patent Application 2007/0025923 A1).

Since these new arguments were never presented before filing of the Appeal Brief, the Examiner did not have an opportunity to respond before the Appeal Brief. Therefore, the following new rejection, Noe et al. (US Patent 6,613,795 B2) in view of Postma et al. ("Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening" *European Respiratory Journal*, 2001; 17: 1083-1088), will now apply. Please note that the new rejection below is substantially similar to the previous rejection of record.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

Noe et al. (US Patent 6,613,795 B2)

Wurst et al. (US Patent Application 2007/0025923 A1)

Postma et al. ("Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening" *European Respiratory Journal*, 2001; 17: 1083-1088)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim(s) 1, 4, 8-11, 19 are rejected under 35 U.S.C. 103(a) as being obvious over Noe et al. (US Patent 6,613,795 B2) in view of Postma et al. ("Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening" *European Respiratory Journal*, 2001; 17: 1083-1088).

The instant claims are directed to a dry powder inhalation product consisting of (3R,2'R)-3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%), ciclesonide, and lactose monohydrate.

Noe et al. teach a method of treating obstructive respiratory diseases, such as asthma and bronchitis, by administering a dry powder formulation consisting of (3R,2'R)-3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%) and lactose monohydrate (examples and claims).

Examiner notes that the limitation drawn to once or twice daily treatment of a clinical condition for which a corticosteroid and/or an anticholinergic agent as well as the limitation drawn to suitable administrations are given little patentable weight since the claims are drawn to a composition. Furthermore, the instant claims do not recite any component in the composition that would distinguish it from a composition that does not recite these limitations.

It is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish from each other. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Thus, the intended use of a composition claim will be given no patentable weight.

It is further respectfully pointed out that a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or

structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). See MPEP 2111.02.

However, Noe et al. fail to disclose ciclesonide.

Postma et al. teaches the treatment of asthma by the inhaled corticosteroid, ciclesonide, which provided significantly improved asthma control (title and abstract).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to combine ciclesonide, as taught by Postma et al. with the composition consisting of (3R,2'R)-3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%) and lactose monohydrate, as taught by Noe et al.

A person of ordinary skill in the art would have been motivated to combine ciclesonide with (3R,2'R)-3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%) and lactose monohydrate because: (1) Postma et al. teaches that the treatment of asthma by administering ciclesonide, which significantly improves asthma control; and (2) Noe et al. teaches a method of treating respiratory disease, such as asthma and bronchitis, by administering (3R,2'R)-3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%) and lactose monohydrate in a dry powder formulation. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating asthma or bronchitis by administering a dry powder formulation consisting of (3R,2'R)-

3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%), ciclesonide, and lactose monohydrate.

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

(10) Response to Argument

Appellant argues that the Wurst et al. reference is not valid prior art because the instant application and the Wurst et al. application were subject to an obligation of assignment to the same entity - "Altana Pharma AG" of Konstanz, Germany. Therefore, the Wurst et al. reference clearly falls within the 35 USC 103(c)(1) exception and does not qualify as prior art against the present application and cannot be relied on to attempt to establish a prima facie case of obviousness.

This is persuasive and accordingly the prima facie case of obviousness of Noe et al. (US Patent 6,613,795 B2) in view of Wurst et al. (US Patent Application 2007/0025923 A1) has been withdrawn. The following new rejection of Noe et al. (US Patent 6,613,795 B2) in view of Postma et al. ("Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening" *European Respiratory Journal*, 2001; 17: 1083-1088) will now apply.

Examiner notes that the two obviousness rejections are substantially similar in that the secondary references (Wurst and Postma et al.) provides the same teaching that ciclesonide is useful for treating asthma.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

This examiner's answer contains a new ground of rejection set forth in section **(9)** above. Accordingly, appellant must within **TWO MONTHS** from the date of this answer exercise one of the following two options to avoid *sua sponte* **dismissal of the appeal** as to the claims subject to the new ground of rejection:

(1) **Reopen prosecution.** Request that prosecution be reopened before the primary examiner by filing a reply under 37 CFR 1.111 with or without amendment, affidavit or other evidence. Any amendment, affidavit or other evidence must be relevant to the new grounds of rejection. A request that complies with 37 CFR 41.39(b)(1) will be entered and considered. Any request that prosecution be reopened will be treated as a request to withdraw the appeal.

(2) **Maintain appeal.** Request that the appeal be maintained by filing a reply brief as set forth in 37 CFR 41.41. Such a reply brief must address each new ground of rejection as set forth in 37 CFR 41.37(c)(1)(vii) and should be in compliance with the other requirements of 37 CFR 41.37(c). If a reply brief filed pursuant to 37 CFR 41.39(b)(2) is accompanied by any amendment, affidavit or

other evidence, it shall be treated as a request that prosecution be reopened before the primary examiner under 37 CFR 41.39(b)(1).

Extensions of time under 37 CFR 1.136(a) are not applicable to the TWO MONTH time period set forth above. See 37 CFR 1.136(b) for extensions of time to reply for patent applications and 37 CFR 1.550(c) for extensions of time to reply for ex parte reexamination proceedings.

A Technology Center Director or designee must personally approve the new ground(s) of rejection set forth in section (9) above by signing below:

/Remy Yucel/

Director, Technology Center 1600

Respectfully submitted,

/Yong S. Chong/

Yong S. Chong
Primary Examiner
Art Unit 1627

ysc
3/4/2011

Conferees:

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627

/Shengjun Wang/

Primary Examiner, Art Unit 1627

Notice of References Cited	Application/Control No. 10/589,871	Applicant(s)/Patent Under Reexamination ROSCHER ET AL.	
	Examiner YONG CHONG	Art Unit 1627	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
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FOREIGN PATENT DOCUMENTS

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NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Postma et al. ("Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening" European Respiratory Journal, 2001; 17: 1083-1088)
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Eur Respir J 2001; 17: 1083–1088
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Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening

D.S. Postma*, C. Sevette#, Y. Martinat¶, N. Schlösser+, J. Aumann§, H. Kafé†

Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening. D.S. Postma, C. Sevette, Y. Martinat, N. Schlösser, J. Aumann, H. Kafé. ©ERS Journals Ltd 2001.

ABSTRACT: The study addressed the question whether the novel inhaled prodrug corticosteroid ciclesonide is equally effective when inhaled in the morning compared to the evening.

For this purpose a double-blind, randomized, parallel group study was initiated in which 209 asthmatic patients (forced expiratory volume in one second = 50–90% predicted) inhaled either 200 µg ciclesonide in the morning or in the evening, for 8 weeks. Efficacy was assessed by means of spirometry as well as daily recordings of morning and evening peak expiratory flow (PEF), symptoms and use of rescue medication. The 24-h urinary cortisol excretion was measured to evaluate any effect on hypothalamic-pituitary-adrenol axis.

Ciclesonide significantly improved asthma control. Morning and evening administration was shown to be equally effective for the different spirometry variables, evening PEF, symptoms, use of rescue medication and number of asthma exacerbations. Regarding morning PEF, the improvements after evening dosing were more prominent and equivalence of morning and evening administration could not be demonstrated. No relevant influence on cortisol excretion was found.

Overall, the study indicates that ciclesonide can be given either in the morning or in the evening to meet the patients' preference and individual medical needs, although evening administration may lead to a more pronounced improvement in morning peak expiratory flow.

Eur Respir J 2001; 17: 1083–1088.

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inhaled steroids
once daily

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The study was supported by Byk Gulden Pharmaceuticals.

Inhaled corticosteroids have become the mainstay of therapy for patients with asthma. However, as with other inhaled or oral asthma drugs, compliance to inhaled steroids is often poor [1]. Among the manifold reasons underlying noncompliance, complicated regimens and dosing frequency are considered to be significant factors. Initially, inhaled steroids were recommended to be used four-times a day. Although such a regimen might be more effective than twice-daily dosing [2], in daily life higher compliance with a twice-daily regimen might well compensate reduced efficacy [3]. Meanwhile numerous studies have shown that in the majority of patients a twice-daily schedule can effectively control asthma and this is presently the standard scheme. Additionally, it was suggested that decreasing the dosing frequency to once daily might further enhance adherence to the prescribed regimen [4]. In the past the efficacy of once-daily administration was, therefore, tested with a number of inhaled steroids in patients with mild-to-moderate asthma [5].

Ciclesonide is a novel prodrug glucocorticosteroid in development for the treatment of asthma. Ciclesonide which has a chiral centre in the acetal side chain, exists as two epimers with different receptor affinities and metabolization rates. Only R-ciclesonide was selected for clinical development (referred to as ciclesonide from now on). Ciclesonide itself is inactive and needs to be cleaved by esterases to bind to the glucocorticoid receptor. The efficacy of ciclesonide in humans was demonstrated in two placebo-controlled trials showing a dose-dependent reduction of airway hyperresponsiveness to adenosine-5′-monophosphate [6] and a significant inhibition of early and late phase reaction after allergen challenge [7].

Ciclesonide is currently developed for once-daily dosing in patients with mild-to-moderate asthma. In the majority of clinical trials carried out so far it was administered as a single dose in the morning and a daily dose of 200 µg was shown to be superior to placebo. In order to tailor asthma management of individuals, a flexible dosing time would be ideal.

The present study, therefore, addressed the question whether the time point of administration (either morning or evening) affects the efficacy of ciclesonide. Based on the results for budesonide [8] the hypothesis was put forward that morning and evening dosing of ciclesonide are equi-effective.

Patients and methods

Patients

Outpatients of either sex, aged 18–75 yrs, with a history of bronchial asthma as defined by American Thoracic Society (ATS) criteria [9] were included.

Patients were eligible to enter the baseline period if they had used rescue medication only during the past 4 weeks and their forced expiratory volume in one second (FEV_1) ranged 50–90% predicted. Patients being pretreated with inhaled steroids (daily doses of up to 500 μg beclomethasone dipropionate (BDP) or flunisolide, 400 μg budesonide and 250 μg fluticasone propionate for at least 4 weeks) were also eligible if their FEV_1 was 80–100% pred. The inhaled steroids were withdrawn at the start of the baseline period. For randomization, FEV_1 had to be 50–90% pred in all patients. In addition, the patients had to show reversibility ($\Delta FEV_1 \geq 15\%$ initial) after inhalation of 200–400 μg salbutamol either during the baseline period or the past 3 months.

Patients were excluded if they had either an asthma exacerbation, an infection of the lower airways, a hospital admission for asthma or if they used systemic steroids in the 4 weeks prior to start of baseline. Patients were also excluded if they suffered from chronic obstructive pulmonary disease (COPD) and/or other relevant lung diseases, or were heavy (ex-) smokers with ≥ 10 pack-yrs. Pregnant, lactating and premenopausal females without safe contraception were ineligible.

Written informed consent was obtained from each patient prior to entering the trial. The protocol was approved by the Ethics Committees of the individual investigators.

Study protocol

The study had a double-blind, randomized, parallel group design. Following a baseline period of 1–4 weeks, the patients were randomly allocated to one of two treatment groups: either ciclesonide in the morning (treatment group "morning") or ciclesonide in the evening (treatment group "evening"). Each patient inhaled one puff of 200 μg ciclesonide at the time point indicated on the label of the inhaler and one puff of placebo at the alternate time point for 8 weeks. Ciclesonide was administered by metered-dose inhaler (MDI) using 1, 1, 1, 2-hydrofluoralkane (HFA) 134a as propellant.

The patients visited the investigational sites at weekly intervals during the baseline period and at 4-weekly intervals during the treatment period or whenever their asthma deteriorated. At each visit lung function was measured and adverse events were elicited by open questioning. At the start of the baseline period, as well as at the end of the treatment period (or upon patient withdrawal), a physical examination including 12-lead electrocardiography (ECG) and a standard safety laboratory work-up was performed. In order to assess the effect of ciclesonide on hypothalamic-pituitary-adrenal (HPA) axis patients collected their 24-h urine at home after 1 week of baseline, as well as at the end of the treatment period and cortisol excretion was determined. Creatinine was also measured in urine to allow for correction in case random or limited time collections were made. The cortisol radioimmunoassay used did not interfere with ciclesonide or its active metabolite.

In an individual subject, all lung function readings (FEV_1, forced vital capacity (FVC)) had to be performed within ± 1.5 h referenced to the randomization visit. The rescue medication had to be withheld for ≥ 4 h prior to each measurement. The highest value from at least three technically satisfactory attempts was used for analysis. Predicted values were calculated according to the formula of the European Coal and Steel Community [10].

No other asthma drugs except rescue medication and trial medication were allowed throughout the trial. Short-acting β-agonists (administered by MDI or powder inhaler) were used to relieve symptoms and the same rescue medication (drug and device) was to be utilized throughout the trial. Cromones (as nasal spray or eyedrops) and histamine 1 receptor (H1)-blockers were allowed to treat symptoms of allergic rhinitis. Nasal and dermatological steroids were not permitted during the 4 weeks before the start of the baseline period as well as during the study. In case treatment with oral steroids became necessary because of an asthma exacerbation, the patient had to be withdrawn from the trial. Those cases were handled as "lack of efficacy" and included in the per-protocol end-point analysis.

Throughout the trial the patients recorded peak expiratory flow (PEF) (Roland® Pulmo-Test AS, Roland Arzneimittel, Hamburg, Germany) daily in the morning, immediately after getting up, and in the evening between 16:00–20:00 h. At the same time symptoms as noted during the night and day, respectively, were recorded applying a four-point scale (*i.e.* the maximum daily score was 8). Additionally, the daily use of the rescue medication had to be documented in a diary. For the diary variables, the mean of all entries made during the week prior to a visit was used for analysis. For the sake of brevity, the average of a weeks measurements of morning PEF are referred to as "morning PEF". The same holds true for accounts of all other diary card variables. Both the investigator and the patient assessed the effectiveness of the trial medication according to a four-point scale: very effective (good control of asthma), effective (not optimal, but acceptable asthma control), slightly effective (moderate asthma control, improvement desired), ineffective (poor control of asthma).

Statistical analysis

Primary efficacy variable was the weekly average of morning PEF (average of last week of study *versus* average of last week of baseline). A sample size of 86 patients per group gives 90% power to correctly conclude equivalence in morning PEF in case of no treatment difference, $\alpha = 0.05$, two-sided, equivalence range of ± 25 $L \cdot min^{-1}$ for the difference in pre/post changes, for which an SD of 50 $L \cdot min^{-1}$ was assumed [11]. Within and between treatment comparisons were based on the differences between end and start of treatment. For lung function variables, equivalence of morning *versus* evening administration was assessed by analysis of covariance with baseline value and age as covariables, and sex and centre as factors.

Table 1. – Patient characteristics

Variable	Itt analysis		pp analysis	
	Morning	Evening	Morning	Evening
Patients n	110	99	88	80
M:F	65:45	49:50	54:34	40:40
Age yrs*	39 (19–75)	38 (18–68)	39 (19–75)	36 (18–68)
Nonsmokers:(Ex-)Smokers	61:49	54:45	49:39	43:37
Pretreated:nonpretreated with ICS	41:69	37:62	31:57	28:52
ICS pretreatment dose in BDP equivalents μg*	500 (50–1000)	500 (200–500)	500 (200–500)	500 (200–500)
FEV_1 % predicted	77±9	77±11	77±9	75±11
Reversibility % baseline	23.5±11	22.8±11	24.5±11	23.8±12
Morning PEF % predicted	90±18	87±20	90±20	86±8

*: Data are presented as median (range). Pretreatment was calculated as 500 μg beclomethasone dipropionate (BDP) = 500 μg flunisolide = 400 μg budesonide = 250 μg fluticasone propionate, irrespective of type of device; Itt: intention-to-treat; pp: per-protocol; ICS: inhaled corticosteroids; FEV_1: forced expiratory volume in one second; PEF: peak expiratory flow.

Equivalence acceptance limits for FEV_1 and FVC changes were chosen as 200 mL. In this equivalence trial, the per-protocol analysis was considered as primary analysis and the intention-to-treat analysis as a secondary one [12]. Treatment differences in the number of drop-outs due to lack of efficacy were analysed by Fisher's exact test. Changes in symptom scores and use of rescue medication were analysed nonparametrically (Wilcoxon-Pratt signed rank test within groups, Mann-Whitney U-Test between groups). Generally, two-sided 95% confidence limits were given for treatment differences. Data are presented as mean±SD unless stated otherwise.

Results

Out of 270 patients enrolled into the baseline period, 209 were randomized. The protocol was violated by 41 patients and these were excluded from the per-protocol analysis which finally comprised 88 patients in the morning group and 80 patients in the evening group (tables 1 and 2 for baseline characteristics). As the study aimed for equivalence, the efficacy results for the per-protocol population are being reported; the results from the intention-to-treat analysis are, however, well in agreement with the per-protocol analysis. With regard to safety, the results refer to all patients randomized who received at least one dose of the trial medication.

Table 2. – Baseline effectiveness variables for patients in the per-protocol analysis

Variable	Morning	Evening
FEV_1 L	2.72±0.67	2.61±0.71
FVC L	3.84±1.01	3.78±1.15
Morning PEF $L \cdot min^{-1}$	446±131	424±117
Evening PEF $L \cdot min^{-1}$	465±123	440±122
Total daily symptom score*	1.57 (0–5.26)	1.57 (0–7.0)
Daily use rescue medication, puffs $24\ h^{-1}$*	1.29 (0–9.0)	1.76 (0–16.83)

*: Data are presented as median (range). For the diary parameters (morning and evening peak expiratory flow (PEF) symptoms, use of rescue medication) the average over the last 7 days prior to start of treatment is being reported. FEV_1: forced expiratory volume in one second; FVC: forced vital capacity.

Morning and evening peak expiratory flow

Compared to the last week of baseline, morning PEF (fig. 1) in the morning group increased by 8 and 3 $L \cdot min^{-1}$ after 4 and 8 weeks of treatment, respectively, which was not significant. In the evening group the improvements at the corresponding time points amounted to 24 and 30 $L \cdot min^{-1}$ ($p < 0.005$) (table 3). The difference between treatments at 8 weeks was significant ($p < 0.05$).

The change in evening PEF after 8 weeks of treatment was 7 $L \cdot min^{-1}$ in the morning group (NS *versus* baseline) and 16 $L \cdot min^{-1}$ ($p < 0.05$) in the evening group (table 3), resulting in a nonsignificant mean difference between treatments of 10 $L \cdot min^{-1}$.

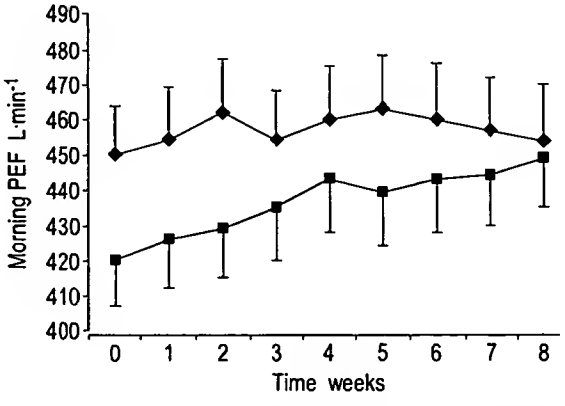

Fig. 1. – Time course mean morning peak expiratory flow (PEF); mean values and SEM. Time point "0" refers to the values recorded during the last week of the baseline period. ◆: morning; ■: evening.

Table 3. – Change in efficacy variables (end *versus* start of 8 weeks treatment)

Variable	Morning	Evening	Morning – evening:
FFEV1 L	0.31 (0.20–0.43)	0.31 (0.19–0.43)	0.00 (-0.15–0.15)
FVC L	0.19 (0.06–0.33)	0.22 (0.08–0.36)	-0.02 (-0.19–0.14)
Morning PEF L·min^{-1}	3 (-14–20)	30 (13–48)	-27 (-50–-5)
Evening PEF L·min^{-1}	7 (-10–23)	16 (0.4–32)	-10 (-31–11)
Total daily symptom score	-0.38 (-0.80–-0.24)	-0.50 (-0.87–-0.29)	0.02 (-0.29–0.43)
Daily use rescue medication, puffs·24 h^{-1}	-0.36 (-1.00–-0.29)	-0.36 (-1.05–-0.21)	0 (-0.43–0.43)

Lung function: least-squares means and 95% confidence intervals (CI); symptoms and rescue medication: within groups; median and 95% CI, between groups: distribution-free point estimate and 95%-CI. FEV1: Forced expiratory volume in one second; FVC: forced vital capacity; PEF: peak expiratory flow.

Spirometry

Compared to the last baseline reading, FEV1 and FVC increased significantly (at least $p<0.05$) after 8 weeks of treatment in both treatment groups (table 3) and morning and evening administration proved to be equally effective. A similar improvement was observed after 4 weeks of treatment with increases amounting to 200 and 300 mL in the morning and evening for FEV1 and 150 and 250 mL for FVC, respectively. The time course of effect separated for patients either pretreated with inhaled steroids or not, is shown in figure 2.

Symptoms

After both morning and evening administration of ciclesonide, total daily asthma symptoms improved significantly (at least $p<0.001$) after 4 (data not shown) and 8 weeks of treatment (table 3). While during baseline only 21% and 24% of patients in the morning and evening group, respectively, were symptom-free, the percentage of patients without symptoms more than doubled (53% and 55%) after 8 weeks of treatment. No significant difference was found between groups for the total daily score as well as for symptoms reported during the day and night, respectively.

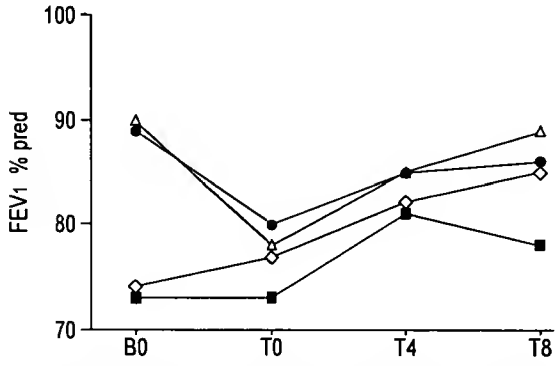

Fig. 2. – Time course in forced expiratory volume in one second (FEV1) in patients either with or without pretreatment with inhaled corticosteroids prior to the study. B0: start of baseline period; T0: time of randomization; T4/T8: after 4/8 weeks of treatment. ◇: morning, not pretreated; ■: evening, not pretreated; ●: morning pretreated; △: evening pretreated.

Use of rescue medication

In both groups the use of rescue medication was significantly (at least $p<0.05$) reduced after 4 (data not shown) and 8 weeks of treatment (table 3). The improvement was comparable in both groups and no significant difference between the groups was found. The same holds true for the percentage of rescue medication free days although this was slightly higher in the morning group (54% *versus* 46% in the evening group).

Lack of efficacy

Lack of efficacy was described in the study protocol as asthma exacerbations to be treated with oral steroids. Eight out of 209 randomized patients (3.8%) in total (four in each group) experienced lack of efficacy.

Efficacy rating

Both the investigators and patients rated ciclesonide as being "very effective" or "effective" in 61% and 63%, respectively, of the patients treated in the morning, and in 71% and 63% with regard to the evening administration.

Safety

Overall, both treatment regimens were safe and well tolerated and there were no differences in the safety aspects between the groups. Eleven patients prematurely left the study because of adverse events; seven in the morning group and four in the evening group. This includes six patients who experienced lack of efficacy as described earlier. The other events leading to withdrawal were one case each of bronchial hypersecretion, nausea/vomiting, dyspnoea and panic attacks, the latter occurring under placebo.

The most frequent adverse events ($\geq 3\%$) concerned the respiratory system (upper respiratory infection: 6.7%; asthma: 6.2%; bronchitis: 4.3%). Two patients (1%) reported voice alterations; no case of candidiasis was described.

Mean 24-h urinary cortisol excretion normalized for creatinine amounted to 8.49 and 8.10 nmol·mmol

creatinine^{-1} (morning and evening group, respectively) during baseline. At the end of treatment, the respective values were 10.47 and 13.88 nmol·mmol creatinine^{-1}. Mean differences within treatment groups (morning: 1.98 nmol·mmol creatinine^{-1} (95% confidence interval (CI): -2.34–6.33); evening: 5.78 nmol·mmol creatinine^{-1} (95% CI: -6.51–18.06)) were not significant as were the differences between treatment groups (-3.80 nmol·mmol creatinine^{-1} (95% CI: -16.79–9.19)). Values below the normal range occurred in 23 patients at baseline and in 15 at the end of the treatment in the morning group, and in 28 and 24 patients, respectively, in the evening group.

Discussion

Results of the present study suggest that 200 μg ciclesonide given once daily is effective in the treatment of mild-to-moderate asthma as assessed by lung function, symptoms, use of rescue medication and number of asthma exacerbations. Although the trial did not have a placebo or active control group, the consistent improvements above baseline values were not only statistically significant but also clinically relevant, and thus support this conclusion.

Morning and evening administration was shown to be equally effective for the different variables, except for morning PEF where the improvements after evening dosing were more prominent. When looking at individual patient responses (see 95% CI in table 3) obviously some patients deteriorated while others improved resulting in no relevant change overall. Hence, the response pattern to a dose given in the morning seems to be more heterogeneous compared to evening administration where all patients had higher values at the end of treatment referred to baseline. It should be noted that baseline morning PEF values in the morning group were higher than in the evening group. It, therefore, might be suspected that a ceiling effect occurred and that the morning group had in fact no room for further improvement. This speculation is, however, not supported by the covariance analysis, which took the differences in baseline into account and nevertheless suggested a significant difference in outcome for the two groups. As two other trials with ciclesonide showed that 100 and 200 μg·day^{-1} given in the morning significantly improved morning PEF compared to placebo, no explanation is, therefore, readily available why this variable was unchanged in the morning group of the current study.

When selecting the optimal time point of administration for an individual patient, the following aspects may be relevant: patient compliance, the fact that asthma can have an important nocturnal component and safety considerations. With regard to compliance, morning dosing of inhaled steroids is favoured [13]. Concerning safety, pharmacokinetic/pharmacodynamic modelling suggests that inhalation of steroids in the afternoon might cause the least cortisol suppression, with the optimum time point being determined by the terminal elimination half-life of the respective drug: *i.e.* an administration time point of 15:00 h was proposed for fluticasone propionate and of 19:00 h for flunisolide [14]. Finally, due to the circadian rhythm in lung function, hyperresponsiveness, circulating cells and mediators in asthma, it might be expected that based on the results with oral and intravenous steroids [15, 16], afternoon/evening dosing of inhaled steroids is preferable to morning dosing for alleviation of nocturnal worsening in asthma.

Morning administration of budesonide was shown to be superior to placebo [17] and the authors concluded that recommendation for the time of dosing may well be left to the individual physician. Several studies evaluated the efficacy of evening dosing of budesonide and with the exception of one trial [4] they all found that evening administration is at least as effective as twice-daily dosing [18–20]. In addition, JONES *et al.* [8] addressed the issue of time of dosing and concluded that morning and evening administration of budesonide are equi-effective. Similar findings were made for flunisolide; although for morning PEF and daytime use of rescue medication there was a trend in favour of evening dosing [21]. The efficacy of 100 μg fluticasone propionate twice-daily was generally greater than a 200 μg once-daily morning regimen in patients pretreated with inhaled steroids, whereas no such difference was seen in patients pretreated with bronchodilators only [22]. Hence, there is clear evidence from the literature that once-daily dosing of inhaled steroids is an effective regimen for the treatment of mild-to-moderate asthma. No final conclusion is yet possible about the ideal time point of administration although some studies suggest that morning dosing might be less efficacious. In fact PINCUS and coworkers [13, 23] proposed that administration of inhaled steroids in the afternoon between 15:00–17:30 h might result in the most pronounced asthma control. However, afternoon administration does not necessarily increase compliance and as the present trial suggests, relevant improvement can also be achieved by evening dosing between 16:00–20:00 h, the time window for optimal administration of inhaled steroids might in fact be wider. This is also in line with a study investigating the efficacy of a single dose of 1,000 μg BDP·day^{-1} in the late afternoon (17:00 h) and at bedtime (22:00 h) showing comparable asthma control for both regimens [24].

The safety data of the current trial suggest that ciclesonide was well tolerated. No influence on HPA axis was found as judged by 24-h urinary cortisol suppression. This is in line with the results of a study in healthy volunteers where the 24-h mesor for serum cortisol under ciclesonide (800 μg), given either in the morning or in the evening for one week, was 2–6% lower compared to placebo indicating that ciclesonide lacks relevant systemic effects [25]. Hence, from a safety point of view ciclesonide can be administered both in the morning or evening.

Although the question on the ideal time point of once-daily administration of inhaled steroids warrants further investigation, the current study suggests that ciclesonide can be given either in the morning or in the evening so that patient preference and individual medical needs can be addressed.

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References

1. Rand CS. Patient and regimen-related factors that influence compliance with asthma therapy. *Eur Respir Rev* 1998; 8: 270–274.
2. Toogood JH, Baskerville JC, Jennings B, Lefcoe NM, Johansson SA. Influence of dosing frequency and schedule on the response of chronic asthmatics to the aerosol steroid budesonide. *J Allergy Clin Immunol* 1982; 70: 288–298.
3. Reed CE. Aerosol glucocorticoid treatment of asthma: adults. *Am Rev Respir Dis* 1990; 141: S82–S88.
4. Weiner P, Weiner M, Azgad Y. Long term clinical comparison of single versus twice daily administration of inhaled budesonide in moderate asthma. *Thorax* 1995; 50: 1270–1273.
5. Campbell LM. Once-daily inhaled corticosteroids in mild to moderate asthma. Improving acceptance of treatment. *Drugs* 1999; 58: Suppl. 4. 25–33.
6. Taylor DA, Jensen MW, Kanabar V, *et al.* A dose-dependent effect of the novel inhaled corticosteroid ciclesonide on airway responsiveness to adenosine-5'-monophosphate in asthmatic patients. *Am J Respir Crit Care Med* 1999; 160: 237–243.
7. Dahl R, Nielsen LP, Christensen MB, Engelstätter R. Ciclesonide - an inhaled corticosteroid prodrug-inhibits allergen induced early and late phase reactions. *Eur Respir J* 1998; 12: Suppl. 28, 62.
8. Jones AH, Langdon CG, Lee PS, *et al.* Pulmicort® Turbohaler® once daily as initial prophylactic therapy of asthma. *Respir Med* 1994; 88: 293–299.
9. American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. *Am Rev Respir Dis* 1987; 136: 225–244.
10. Quanjer PH, Dalhuijsen A, van Zomeren BC. Summary equations of reference values. *Bull Eur Physiopathol Respir* 1993; 19: Suppl. 5, 45–51.
11. Davies RJ, Stampone P, O'Connor BJ. Hydrofluoroalkane-134a beclomethasone dipropionate extrafine aerosol provides equivalent asthma control to chlorofluorocarbon beclomethasone dipropionate at approximately half the total daily dose. *Respir Med* 1998; 92: Suppl. A, 23–31.
12. International conference on harmonisation of technical requirements for registration of pharmaceuticals for human use. ICH harmonised tripartitate guideline: statistical principles for clinical trials. *Statist Med* 1999; 18: 1905–1942.
13. Pincus DJ, Humeston TR, Martin RJ. Further studies on the chronotherapy of asthma with inhaled steroids: the effect of dosage timing on drug efficacy. *J Allergy Clin Immunol* 1997; 100: 771–774.
14. Maibohm B, Hochhaus G, Rohatagi S, *et al.* Dependency of cortisol suppression on the administration time of inhaled corticosteroids. *J Clin Pharmacol* 1997; 37: 704–710.
15. Beam WR, Ballard RD, Martin RJ. Spectrum of corticoid sensitivity in nocturnal asthma. *Am Rev Respir Dis* 1992; 145: 1082–1086.
16. Beam WR, Weiner DE, Martin RJ. Timing of prednisolone and alterations of airway inflammation in nocturnal asthma. *Am Rev Respir Dis* 1992; 146: 1524–1530.
17. McFadden ER, Casale TB, Edwards TB, *et al.* Administration of budesonide once daily by means of Turbuhaler to subjects with stable asthma. *J Allergy Clin Immunol* 1999; 104: 46–52.
18. Campbell LM, Gunn SD, Sweeney D, *et al.* Once daily budesonide: effective control of moderately severe asthma with 800 mcg once daily inhaled via Turbohaler when compared with 400 µg twice daily. *Eur J Clin Res* 1995; 7: 1–14.
19. Venables TL, Addlestone MB, Smithers AJ, *et al.* A comparison of the efficacy and patient acceptability of 20 once daily budesonide via Turbohaler and twice daily fluticasone propionate via disk-inhaler in an equal daily dose of 400 µg in adult asthmatics. *Br J Clin Res* 1996; 7: 15–32.
20. Campbell LM, Bodalia B, Gogbashian CA, Gunn SD, Humphreys PJ, Powell JP. Once-daily budesonide: 400 µg once daily is as effective as 200 µg twice daily in controlling childhood asthma. *Int J Clin Pract* 1998; 52: 213–219.
21. ZuWallack RL, Rosen JP, Cohen L, *et al.* The effectiveness of once-daily dosing of inhaled flunisolide in maintaining asthma control. *J Allergy Clin Immunol* 1997; 99: 278–285.
22. Wolfe J, Rooklin A, Grady J, *et al.* Comparison of once- and twice-daily dosing of fluticasone propionate 200 micrograms per day administered by Diskus device in patients with asthma treated with or without inhaled corticosteroids. *J Allergy Clin Immunol* 2000; 105: 1153–1161.
23. Pincus DJ, Szefler SJ, Ackerson LM, Martin RJ. Chronotherapy of asthma with inhaled steroids: the effect of dosage timing on drug efficacy. *J Allergy Clin Immunol* 1995; 95: 1172–1178.
24. Gagnon M, Côte J, Milot J, Turcotte H, Boulet L-P. Comparative safety and efficacy of single or twice daily administration of inhaled beclomethasone in moderate asthma. *Chest* 1994; 105: 1732–1737.
25. Weinbrenner A, Hüneke D, Zschiesche M, *et al.* Circadian rhythm of serum cortisol after repeated inhalation of the new topical steroid ciclesonide. *Eur J Clin Pharmacol* 1998; 54: A27.

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CHONG, YONG SOO	
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The time period for reply, if any, is set in the attached communication.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/589,871
Filing Date: August 18, 2006
Appellant(s): ROSCHER ET AL.

Joshua B. Goldberg
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 1/26/2011 appealing from the Office action mailed 1/5/2010.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of the claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The 103(a) obviousness rejection of claims 1, 4, 8-11, 19 as being obvious over Noe et al. (US Patent 6,613,795 B2) in view of Wurst et al. (US Patent Application 2007/0025923 A1) was made in the Final Rejection filed on 1/5/2010 as necessitated by the new claim amendments.

Appellant made new grounds of arguments in the Appeal Brief filed on 1/26/2011, which were persuasive to withdraw the 103(a) obviousness rejection

of claims 1, 4, 8-11, 19 as being obvious over Noe et al. (US Patent 6,613,795 B2) in view of Wurst et al. (US Patent Application 2007/0025923 A1).

Since these new arguments were never presented before filing of the Appeal Brief, the Examiner did not have an opportunity to respond before the Appeal Brief. Therefore, the following new rejection, Noe et al. (US Patent 6,613,795 B2) in view of Postma et al. ("Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening" *European Respiratory Journal*, 2001; 17: 1083-1088), will now apply. Please note that the new rejection below is substantially similar to the previous rejection of record.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

Noe et al. (US Patent 6,613,795 B2)

Wurst et al. (US Patent Application 2007/0025923 A1)

Postma et al. ("Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening" *European Respiratory Journal*, 2001; 17: 1083-1088)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim(s) 1, 4, 8-11, 19 are rejected under 35 U.S.C. 103(a) as being obvious over Noe et al. (US Patent 6,613,795 B2) in view of Postma et al. ("Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening" *European Respiratory Journal*, 2001; 17: 1083-1088).

The instant claims are directed to a dry powder inhalation product consisting of (3R,2'R)-3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%), ciclesonide, and lactose monohydrate.

Noe et al. teach a method of treating obstructive respiratory diseases, such as asthma and bronchitis, by administering a dry powder formulation consisting of (3R,2'R)-3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%) and lactose monohydrate (examples and claims).

Examiner notes that the limitation drawn to once or twice daily treatment of a clinical condition for which a corticosteroid and/or an anticholinergic agent as well as the limitation drawn to suitable administrations are given little patentable weight since the claims are drawn to a composition. Furthermore, the instant claims do not recite any component in the composition that would distinguish it from a composition that does not recite these limitations.

It is respectfully pointed out that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish from each other. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Thus, the intended use of a composition claim will be given no patentable weight.

It is further respectfully pointed out that a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or

structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). See MPEP 2111.02.

However, Noe et al. fail to disclose ciclesonide.

Postma et al. teaches the treatment of asthma by the inhaled corticosteroid, ciclesonide, which provided significantly improved asthma control (title and abstract).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to combine ciclesonide, as taught by Postma et al. with the composition consisting of (3R,2'R)-3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%) and lactose monohydrate, as taught by Noe et al.

A person of ordinary skill in the art would have been motivated to combine ciclesonide with (3R,2'R)-3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%) and lactose monohydrate because: (1) Postma et al. teaches that the treatment of asthma by administering ciclesonide, which significantly improves asthma control; and (2) Noe et al. teaches a method of treating respiratory disease, such as asthma and bronchitis, by administering (3R,2'R)-3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%) and lactose monohydrate in a dry powder formulation. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating asthma or bronchitis by administering a dry powder formulation consisting of (3R,2'R)-

3[(cyclopentylhydroxyphenylacetyl)oxy]-1,1-dimethylpyrrolidium bromide (with a minimum ee of 90%), ciclesonide, and lactose monohydrate.

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

(10) Response to Argument

Appellant argues that the Wurst et al. reference is not valid prior art because the instant application and the Wurst et al. application were subject to an obligation of assignment to the same entity - "Altana Pharma AG" of Konstanz, Germany. Therefore, the Wurst et al. reference clearly falls within the 35 USC 103(c)(1) exception and does not qualify as prior art against the present application and cannot be relied on to attempt to establish a prima facie case of obviousness.

This is persuasive and accordingly the prima facie case of obviousness of Noe et al. (US Patent 6,613,795 B2) in view of Wurst et al. (US Patent Application 2007/0025923 A1) has been withdrawn. The following new rejection of Noe et al. (US Patent 6,613,795 B2) in view of Postma et al. ("Treatment of asthma by the inhaled corticosteroid ciclesonide given either in the morning or evening" *European Respiratory Journal*, 2001; 17: 1083-1088) will now apply.

Examiner notes that the two obviousness rejections are substantially similar in that the secondary references (Wurst and Postma et al.) provides the same teaching that ciclesonide is useful for treating asthma.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

This examiner's answer contains a new ground of rejection set forth in section **(9)** above. Accordingly, appellant must within **TWO MONTHS** from the date of this answer exercise one of the following two options to avoid *sua sponte* **dismissal of the appeal** as to the claims subject to the new ground of rejection:

(1) **Reopen prosecution.** Request that prosecution be reopened before the primary examiner by filing a reply under 37 CFR 1.111 with or without amendment, affidavit or other evidence. Any amendment, affidavit or other evidence must be relevant to the new grounds of rejection. A request that complies with 37 CFR 41.39(b)(1) will be entered and considered. Any request that prosecution be reopened will be treated as a request to withdraw the appeal.

(2) **Maintain appeal.** Request that the appeal be maintained by filing a reply brief as set forth in 37 CFR 41.41. Such a reply brief must address each new ground of rejection as set forth in 37 CFR 41.37(c)(1)(vii) and should be in compliance with the other requirements of 37 CFR 41.37(c). If a reply brief filed pursuant to 37 CFR 41.39(b)(2) is accompanied by any amendment, affidavit or

other evidence, it shall be treated as a request that prosecution be reopened before the primary examiner under 37 CFR 41.39(b)(1).

Extensions of time under 37 CFR 1.136(a) are not applicable to the TWO MONTH time period set forth above. See 37 CFR 1.136(b) for extensions of time to reply for patent applications and 37 CFR 1.550(c) for extensions of time to reply for ex parte reexamination proceedings.

A Technology Center Director or designee must personally approve the new ground(s) of rejection set forth in section (9) above by signing below:

/Remy Yucel/

Director, Technology Center 1600

Respectfully submitted,

/Yong S. Chong/

Yong S. Chong
Primary Examiner
Art Unit 1627

ysc
3/4/2011

Conferees:

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Primary Examiner, Art Unit 1627